WEST Search History

DATE: Wednesday, August 21, 2002

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT; PLUR=YES; OP=ADJ		
L4	L3 same (stenosis or (obstruct$5 same arter$5))	2	L4
L3	collagenase	5607	L3
L2	L1 and collagen$5	1	L2
L1	6074659.pn.	1	L1

END OF SEARCH HISTORY

Case Creation Option

Case "09669051" already exists. Please overwrite it or cancel the operation.

The Contents of Case *"09669051"*

Qnum	Query	DB Name	Thesaurus	Operator	Plural
Q1	((424/94.64)!.CCLS.)	USPT	None	ADJ	YES
Q2	(((424/423)!.CCLS.))	USPT	None	ADJ	YES
Q3	(((424/424)!.CCLS.))	USPT	None	ADJ	YES
Q4	(((424/425)!.CCLS.))	USPT	None	ADJ	YES
Q5	Q1 and Q4	USPT	None	ADJ	YES
Q6	Q2 and Q4	USPT	None	ADJ	YES
Q7	Q3 and Q6	USPT	None	ADJ	YES
Q8	Q1 and Q7	USPT	None	ADJ	YES
Q9	Q1 and Q2	USPT	None	ADJ	YES
Q10	Q3 and Q9	USPT	None	ADJ	YES
Q11	Q6 and Q9	USPT	None	ADJ	YES
Q12	Q4 and Q9	USPT	None	ADJ	YES
Q13	Q7 and Q9	USPT	None	ADJ	YES
Q14	514/1	USPT	None	ADJ	YES
Q15	514/12	USPT	None	ADJ	YES
Q16	514/21	USPT	None	ADJ	YES
Q17	514/232.5	USPT	None	ADJ	YES
Q18	514/232.8	USPT	None	ADJ	YES
Q19	514/234.8	USPT	None	ADJ	YES
Q20	514/255	USPT	None	ADJ	YES
Q21	514/259	USPT	None	ADJ	YES
Q22	514/319	USPT	None	ADJ	YES
Q23	514/324	USPT	None	ADJ	YES
Q24	514/411	USPT	None	ADJ	YES

Q25	514/422	USPT	None	ADJ	YES
Q26	514/428	USPT	None	ADJ	YES
Q27	514/429	USPT	None	ADJ	YES
Q28	514/441	USPT	None	ADJ	YES
Q29	514/449	USPT	None	ADJ	YES
Q30	514/473	USPT	None	ADJ	YES
Q31	Q29 and Q30	USPT	None	ADJ	YES
Q32	Q28 and Q31	USPT	None	ADJ	YES
Q33	Q27 and Q31	USPT	None	ADJ	YES
Q34	Q26 and Q31	USPT	None	ADJ	YES
Q35	Q25 and Q31	USPT	None	ADJ	YES
Q36	Q14 and Q15	USPT	None	ADJ	YES
Q37	Q16 and Q36	USPT	None	ADJ	YES
Q38	Q9 and Q37	USPT	None	ADJ	YES
Q39	Q17 and Q18	USPT	None	ADJ	YES
Q40	Q19 and Q39	USPT	None	ADJ	YES
Q41	Q20 and Q21	USPT	None	ADJ	YES
Q42	Q41 and Q22	USPT	None	ADJ	YES
Q43	Q23 and Q42	USPT	None	ADJ	YES
Q44	Q24 and Q43	USPT	None	ADJ	YES
Q45	Q24 and Q25	USPT	None	ADJ	YES
Q46	Q26 and Q45	USPT	None	ADJ	YES
Q47	Q27 and Q46	USPT	None	ADJ	YES
Q48	Q28 and Q47	USPT	None	ADJ	YES
Q49	Q29 and Q47	USPT	None	ADJ	YES
Q50	Q30 and Q47	USPT	None	ADJ	YES
Q51	Q31 and Q47	USPT	None	ADJ	YES
Q52	Q31 and Q7	USPT	None	ADJ	YES
Q53	Q31 and 40	USPT	None	ADJ	YES
Q54	Q7 and Q53	USPT	None	ADJ	YES
	((biological conduit or artery or vasculature) same (human or mammal or animal)) near5				

Q55	((dilat$5 or open or de-obstruct)near5 (collagenase or protease or collagen degrading enzyme))	USPT,PGPB,JPAB,EPAB,DWPI	None	ADJ	YES
Q56	((biological conduit or artery or vasculature) near5 (human or mammal or animal)) near5 ((dilat$5 or open or de-obstruct)near5 (collagenase or protease or collagen degrading enzyme))	USPT,PGPB,JPAB,EPAB,DWPI	None	ADJ	YES
Q57	((biological conduit or artery or vasculature) near5 (human or mammal or animal)) near5 (dilat$5 or open or de-obstruct)	USPT,PGPB,JPAB,EPAB,DWPI	None	ADJ	YES
Q58	((stenosis or biological conduit or artery or vasculature) near5 (human or mammal or animal)) near5 (dilat$5 or open or de-obstruct)	USPT,PGPB,JPAB,EPAB,DWPI	None	ADJ	YES
Q59	(collagenase or protease or collagen degrading enzyme)	USPT,PGPB,JPAB,EPAB,DWPI	None	ADJ	YES
Q60	Q58 and Q59	USPT,PGPB,JPAB,EPAB,DWPI	None	ADJ	YES
Q61	(collagenase or protease) near5 (((stenosis or biological conduit or artery or vasculature) near5 (human or mammal or animal)) near5 (dilat$5 or open or de-obstruct))	USPT,PGPB,JPAB,EPAB,DWPI	None	ADJ	YES
Q62	collagenase or collagen degrading enzyme or collagen hydrolyzing enzyme	USPT,PGPB,JPAB,EPAB,DWPI	None	ADJ	YES
Q63	Q62 and Q59	USPT,PGPB,JPAB,EPAB,DWPI	None	ADJ	YES
Q64	Q58 and Q63	USPT,PGPB,JPAB,EPAB,DWPI	None	ADJ	YES

WEST Search History

DATE: Thursday, August 15, 2002

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ		
L64	L58 and L63	1	L64
L63	L62 and L59	7841	L63
L62	collagenase or collagen degrading enzyme or collagen hydrolyzing enzyme	7841	L62
L61	(collagenase or protease) near5 (((stenosis or biological conduit or artery or vasculature) near5 (human or mammal or animal)) near5 (dilat$5 or open or de-obstruct))	0	L61
L60	L58 and L59	5	L60
L59	(collagenase or protease or collagen degrading enzyme)	51146	L59
L58	((stenosis or biological conduit or artery or vasculature) near5 (human or mammal or animal)) near5 (dilat$5 or open or de-obstruct)	110	L58
L57	((biological conduit or artery or vasculature) near5 (human or mammal or animal)) near5 (dilat$5 or open or de-obstruct)	86	L57
L56	((biological conduit or artery or vasculature) near5 (human or mammal or animal)) near5 ((dilat$5 or open or de-obstruct)near5 (collagenase or protease or collagen degrading enzyme))	0	L56
L55	((biological conduit or artery or vasculature) same (human or mammal or animal)) near5 ((dilat$5 or open or de-obstruct)near5 (collagenase or protease or collagen degrading enzyme))	0	L55
	DB=USPT; PLUR=YES; OP=ADJ		
L54	L7 and L53	0	L54
L53	L31 and 40	5	L53
L52	L31 and L7	0	L52
L51	L31 and L47	0	L51
L50	L30 and L47	0	L50
L49	L29 and L47	0	L49
L48	L28 and L47	0	L48
L47	L27 and L46	4	L47
L46	L26 and L45	14	L46
L45	L24 and L25	52	L45
L44	L24 and L43	0	L44
L43	L23 and L42	3	L43
L42	L41 and L22	7	L42
L41	L20 and L21	97	L41
L40	L19 and L39	1	L40

L39	L17 and L18	47	L39
L38	L9 and L37	0	L38
L37	L16 and L36	2	L37
L36	L14 and L15	27	L36
L35	L25 and L31	0	L35
L34	L26 and L31	0	L34
L33	L27 and L31	0	L33
L32	L28 and L31	0	L32
L31	L29 and L30	6	L31
L30	514/473	635	L30
L29	514/449	686	L29
L28	514/441	111	L28
L27	514/429	257	L27
L26	514/428	822	L26
L25	514/422	1721	L25
L24	514/411	849	L24
L23	514/324	607	L23
L22	514/319	603	L22
L21	514/259	866	L21
L20	514/255	2697	L20
L19	514/234.8	70	L19
L18	514/232.8	501	L18
L17	514/232.5	253	L17
L16	514/21	3606	L16
L15	514/12	6253	L15
L14	514/1	267	L14
L13	L7 and L9	0	L13
L12	L4 and L9	0	L12
L11	L6 and L9	0	L11
L10	L3 and L9	0	L10
L9	L1 and L2	9	L9
L8	L1 and L7	0	L8
L7	L3 and L6	74	L7
L6	L2 and L4	113	L6
L5	L1 and L4	0	L5
L4	(((424/425)!.CCLS.))	257	L4
L3	(((424/424)!.CCLS.))	436	L3
L2	(((424/423)!.CCLS.))	1210	L2
L1	((424/94.64)!.CCLS.)	578	L1

FILE 'CAPLUS' ENTERED AT 15:29:58 ON 15 AUG 2002
L1 3616 (STENOSIS OR BLOCKED BIOLOGICAL CONDUIT OR BLOCKED ARTERY OR
BL
L2 2056712 HUMAN OR MAMMAL OR ANIMAL
L3 246359 DILAT? OR OPEN OR DE-OBSTRUCT
L4 96859 METALLOPROTEASE OR COLLAGENASE OR PROTEASE OR COLLAGEN
DEGRADIN
L5 1636 L1 AND L2
L6 124 L3 AND L5
L7 1 L4 AND L6

FILE 'MEDLINE, BIOSIS, BIOTECHDS, BIOTECHNO, AGRICOLA, EMBASE,
SCISEARCH,
CABA, CEABA-VTB, CONFSCI, NTIS' ENTERED AT 15:34:11 ON 15 AUG 2002
L8 241045 L1
L9 24 L7
L10 114 COLLAGENASE AND ((EXTRACELLULAR MATRIX OR ARTERIAL BLOCKAGE
OR
L11 0 L9 AND L10
L12 96 L10 AND L2
L13 85 L12 AND L3
L14 85 L4 AND L13
L15 0 L5 AND L14
L16 0 L7 AND L14
L17 15 DUP REM L9 (9 DUPLICATES REMOVED)

=> D ABS, BIB l17 6

L17 ANSWER 6 OF 15 SCISEARCH COPYRIGHT 2002 ISI (R)
AB In chronic congestive heart failure, an illness affecting more than 4
million Americans, there is extensive myocardial extracellular matrix
(ECM) remodeling. Failing **human** ventricular myocardium contains
activated matrix metalloproteinases (MMPs) which are involved in adverse
ECM remodeling. Our studies support the concept that impaired ECM
remodeling and MMP activation are, in part, responsible for the cardiac
structural deformation during heart failure. There is no known program
which has declared its aim the investigation of regulation of fibrosis in
hypertrophy and disruption of ECM in cardiac **dilatation** and
failure. The development of transgenic technology, and emerging
techniques
for in vivo gene transfer, suggest a strategy for improving cardiac
function by overexpressing or down regulation of the ECM components such
as MMPs, tissue inhibitor of metalloproteinases (TIMPs), transforming
growth factor beta 1 (TGF beta), decorin, collagen, and integrins in
heart
failure. (C) 1998 by Elsevier Science Inc.
AN 1998:426031 SCISEARCH
GA The Genuine Article (R) Number: ZQ432
TI Dynamic role of extracellular matrix metalloproteinases in heart failure
AU Tyagi S C (Reprint)
CS UNIV MISSISSIPPI, MED CTR, DEPT PHYSIOL & BIOPHYS, JACKSON, MS 39216
(Reprint); UNIV MISSISSIPPI, MED CTR, CTR EXCELLENCE CARDIOVASC RENAL
RES,
JACKSON, MS 39216
CYA USA
SO CARDIOVASCULAR PATHOLOGY, (MAY-JUN 1998) Vol. 7, No. 3, pp. 153-159.
Publisher: ELSEVIER SCIENCE INC, 655 AVENUE OF THE AMERICAS, NEW YORK, NY
10010.

WEST

End of Result Set

Generate Collection | Print

L2: Entry 1 of 1 File: USPT Jun 13, 2000

DOCUMENT-IDENTIFIER: US 6074659 A
TITLE: Therapeutic inhibitor of vascular smooth muscle cells

US PATENT NO. (1):
6074659

Brief Summary Text (11):
In one aspect of the invention, new therapeutic methods and therapeutic conjugates are provided for inhibiting vascular smooth muscle cells in a mammalian host. The therapeutic conjugates contain a vascular smooth muscle binding protein or peptide that binds in a specific manner to the cell membranes of a vascular smooth muscle cell or an interstitial matrix binding protein/peptide that binds in a specific manner to interstitial matrix (e.g., collagen) of the artery wall, coupled to a therapeutic agent that inhibits the activity of the cell. In one embodiment, inhibition of cellular activity results in reducing, delaying, or eliminating stenosis after angioplasty or other vascular surgical procedures. The therapeutic conjugates of the invention achieve these advantageous effects by associating with vascular smooth muscle cells and pericytes, which may transform into smooth muscle cells. The therapeutic conjugate may contain: (1) therapeutic agents that alter cellular metabolism or are inhibitors of protein synthesis, cellular proliferation, or cell migration; (2) microtubule and microfilament inhibitors that affect morphology or increases in cell volume; and/or (3) inhibitors of extracellular matrix synthesis or secretion. In one representative embodiment, the conjugates include a cytotoxic therapeutic agent that is a sesquiterpenoid mycotoxin such as a verrucarin or a roridin. Other embodiments involve cytostatic therapeutic agents that inhibit DNA synthesis and proliferation at doses that have a minimal effect on protein synthesis such as protein kinase inhibitors (e.g., staurosporin), suramin, transforming growth factor-beta (TGF-beta) activators or production stimulators such as trans-2-[4-(1,2-diphenyl-1-butenyl)phenoxy]-N,N- dimethylethylamine (tamoxifen), TGF-beta itself, and nitric oxide releasing compounds (e.g., nitroglycerin) or analogs or functional equivalents thereof. Other moieties that inhibit cell division and are, therefore, useful in the practice of the present invention, include, for example, taxol and analogs thereof such as taxotere. In addition, therapeutic agents that inhibit the contraction or migration of smooth muscle cells and maintain an enlarged luminal area following, for example, angioplasty trauma (e.g., the cytochalasins, such as cytochalasin B, cytochalasin C, cytochalasin D, taxol or analogs thereof such as taxotere or the like) are also contemplated for use in accordance with the present invention. Other aspects of the invention relate to vascular smooth muscle binding proteins that specifically associate with a chondroitin sulfate proteoglycan (CSPG) expressed on the membranes of a vascular smooth muscle cell, and in a preferred embodiment this CSPG has a molecular weight of about 250 kDaltons. In preferred embodiments the vascular smooth muscle binding protein binds to a CSPG target on the cell surface with an association constant of at least 10.sup.-4 M. In another preferred embodiment, the vascular smooth muscle binding protein contains a sequence of amino acids found in the Fab, Fv or CDR (complementarity determining regions) of monoclonal antibody NR-AN-01 or functional equivalents thereof.

Brief Summary Text (17):
The dosage forms of the present invention are optionally targeted to a relevant target cell population by a binding protein or peptide. Preferred binding proteins/peptides of the present invention are vascular smooth muscle cell binding protein, tumor cell

binding protein and immune system effector cell binding protein. Preferred vascular smooth muscle cell binding proteins specifically associate with a chondroitin sulfate proteoglycan (CSPG) expressed on the membranes of a vascular smooth muscle cell, and in a preferred embodiment this CSPG has a molecular weight of about 250 kDaltons. In preferred embodiments, the vascular smooth muscle binding protein binds to a CSPG target on the cell surface with an association constant of at least 10.sup.-4 M. In other preferred embodiments, the vascular smooth muscle binding protein contains a sequence of amino acids found in the Fab, Fv or CDR (complementarity determining regions) of monoclonal antibody NR-AN-01 or functional equivalents thereof. Other preferred binding peptides useful in this embodiment of the present invention include those that localize to intercellular stroma and matrix located between and among vascular smooth muscle cells. Preferred binding peptides of this type are specifically associated with collagen, reticulum fibers or other intercellular matrix compounds. Preferred tumor cell binding proteins are associated with surface cell markers expressed by the target tumor cell population or cytoplasmic epitopes thereof. Preferred immune system-modulated target cell binding proteins are associated with cell surface markers of the target immune system effector cells or cytoplasmic epitopes thereof. Binding peptides/proteins of the present invention also target pathologically proliferating normal tissues.

Detailed Description Text (49):
Other preferred binding peptides useful in targeting the dosage form embodiment of the present invention include those that localize to intercellular stroma and matrix located between and among vascular smooth muscle cells. Such binding peptides deliver the therapeutic agent to the interstitial space between the target cells. The therapeutic agent is released into such interstitial spaces for subsequent uptake by the vascular smooth muscle cells. Preferred binding peptides of this type are associated with epitopes on collagen, extracellular glycoproteins such as tenascin, reticulum and elastic fibers and other intercellular matrix material.

Detailed Description Text (51):
Therapeutic agents of the invention are selected to inhibit a cellular activity of a vascular smooth muscle cell, e.g., proliferation, migration, increase in cell volume, increase in extracellular matrix synthesis (e.g., collagens, proteoglycans, and the like), or secretion of extracellular matrix materials by the cell. Preferably, the therapeutic agent acts either: a) as a "cytostatic agent" to prevent or delay cell division in proliferating cells by inhibiting replication of DNA (e.g., a drug such as adriamycin, staurosporin, tamoxifen or the like), or by inhibiting spindle fiber formation (e.g., a drug such as colchicine) and the like; or b) as an inhibitor of migration of vascular smooth muscle cells from the medial wall into the intima, e.g., an "anti-migratory agent" such as a cytochalasin; or c) as an inhibitor of the intracellular increase in cell volume (i.e., the tissue volume occupied by a cell; a "cytoskeletal inhibitor" or "metabolic inhibitor"); or d) as an inhibitor that blocks cellular protein synthesis and/or secretion or organization of extracellular matrix (i.e., an "anti-matrix agent" such as tamoxifen).

Detailed Description Text (53):
Representative examples of "anti-migratory agents" include inhibitors (i.e., agonists and antagonists, and competitive or non-competitive inhibitors) of chemotactic factors and their receptors (e.g., complement chemotaxins such as C5a, C5a desarg or C4a; extracellular matrix factors, e.g., collagen degradation fragments), or of intracellular cytoskeletal proteins involved in locomotion (e.g., actin, cytoskeletal elements, and phosphatases and kinases involved in locomotion). Representative examples of useful therapeutic agents in this category of anti-migratory agents include: caffeic acid derivatives and nilvadipine (a calcium antagonist), and steroid hormones. Preferred anti-migratory therapeutic agents are the cytochalasins.

Detailed Description Text (59):
Representative examples of "anti-matrix agents" include inhibitors (i.e., agonists and antagonists and competitive and non-competitive inhibitors) of matrix synthesis, secretion and assembly, organizational cross-linking (e.g., transglutaminases cross-linking collagen), and matrix remodeling (e.g., following wound healing). A representative example of a useful therapeutic agent in this category of anti-matrix agents is colchicine, an inhibitor of secretion of extracellular matrix. Another example is tamoxifen for which evidence exists regarding its capability to organize

and/or stabilize as well as diminish smooth muscle cell proliferation following angioplasty. The organization or stabilization may stem from the blockage of vascular smooth muscle cell maturation in to a pathologically proliferating form.

Detailed Description Text (69):
Also contemplated as useful binding peptides for restenosis treatment sustained release dosage forms of the present invention are those that localize to intercellular stroma and matrix located between and among vascular smooth muscle cells. Such binding peptides deliver the therapeutic agent to the interstitial space between the target cells. The therapeutic agent is released into such interstitial spaces for subsequent uptake by the vascular smooth muscle cells. Preferred binding peptides of this type are associated with epitopes on collagen, extracellular glycoproteins such as tenascin, reticulum and elastic fibers, cytokeratin and other intercellular matrix components. Minimal peptides, mimetic organic chemical compounds, human or humanized monoclonal antibodies and the like that localize to intracellular stroma and matrix are also useful as binding peptides in this embodiment of the present invention. Such binding peptides may be identified and constructed or isolated in accordance with known techniques. In preferred embodiments of the present invention, the interstitial matrix binding protein binds to a target epitope with an association constant of at least about 10.sup.-4 M.

Detailed Description Text (198):
FIG. 1B illustrates the binding of NR-AN-01 (a murine IgG2b MAb) to the smooth muscle cells in the vascular wall of an artery in a 24-year old male patient, 4 days after the i.v. administration of NR-AN-01. FIG. 1B is a photomicrograph of a histological section taken through the medial region of an arterial wall of the patient after NR-AN-01 administration, where the section was reacted ex vivo with HRP-conjugated goat anti-mouse IgG. The reaction of the HRP-conjugate with NR-AN-01 MAb was visualized by adding 4-chloro-1-naphthol or 3,3'-diaminobenzidine tetrahydrochloride as a peroxidase substrate (chromogen). The reaction product of the substrate forms an insoluble purple or dark brown precipitate at the reaction site (shown at #2, FIG. 1B). A counter stain was used to visualize collagenous extracellular matrix material (shown at #2, FIG. 1B) or cell nuclei (#1, FIG. 1). Smooth muscle cells are visualized under microscopic examination as purple stained cells (FIG. 1A and FIG. 1B). This photomicrograph (FIG. 1B) demonstrates the ability of the MAb to specifically bind to human vascular smooth muscle in vivo, and to be internalized by the cells and remain in the cells for extended periods.

Detailed Description Text (403):
Rat adventitial fibroblasts were cultured as described in Grainger et al., Biochem. J., 283: 403-408, 1992. Briefly, the aortae were treated with collagenase (3 mg/ml) for 30 minutes at 37.degree. C. The tunica adventitia was stripped away from the media. The adventitia was dispersed for 2 hours in elastase (1 mg/ml) and collagenase (3 mg/ml) dissolved in medium M199 (available from ICN/Flow). The cells were then spun out (900.times.g, 3 minutes), resuspended in DMEM+10% FCS and plated out at 8.times.10.sup.4 cells/cm.sup.2 on tissue culture plastic. When the cells reached confluence (after about 10 days), they were subcultured as described for vascular smooth muscle cells. Adventitial fibroblasts were subcultured every 3 days at 1:3 dilution and used between passages 3 and 9.

Other Reference Publication (118):
Rauterberg et al., "Collagens in Atherosclerotic Vessel Wall Lesions", Current Topics in Pathology, 87, 163-192 (1993).